REMARKS

Claims 125-186 are pending in this application. Response and amendments, filed on August 26, 2009, rendered all previous rejections moot in view of the new grounds of rejections. None of the claims are amended. However, applicants provide a clean set of pending claims for the examiner's convenience. The Office Action is discussed below:

Obviousness Rejections:

On pages 2-14 and 15-16 of the Office Action, the examiner rejects the claims under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), and further in view of Burstein *et al.* (US 6,620,198), and/or Mckellop *et al.* (WO 99/52474), and/or Muratoglu *et al.* (US 2003/0149125), and/or Saum *et al.* (US 2002/0107300).

On pages 2-5 of the Office Action, the examiner rejects claims 125-127, 129-134, 136, 138-140, 142-146, 148, and 151 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315).

On page 6 of the Office Action, the examiner rejects claim 141 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), as applied to claim 125 above, and further in view of Mckellop *et al.* (WO 99/52474).

On pages 6-7 of the Office Action, the examiner rejects claims 149-152 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), as applied to claim 125 above, in further view of Muratoglu *et al.* (US 2003/0149125).

On pages 7-8 of the Office Action, the examiner rejects claims 128 and 153-154 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), as applied to claim 125 above, in further view of Burstein *et al.* (US 6,620,198).

On pages 8-9 of the Office Action, the examiner rejects claims 155-159 and 166-168 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US

6,448,315).

On pages 9-10 of the Office Action, the examiner rejects claim 169 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), as applied to claim 167 above, in further view of Saum *et al.* (US 2002/0107300).

On pages 10-11 of the Office Action, the examiner rejects the claims 160-165 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), as applied to claim 155 above, and further in view of Mckellop *et al.* (WO 99/52474).

On pages 11-13 of the Office Action, the examiner rejects the claims 170-174, 181-185 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), as applied to claim 125 above, in further view of Burstein *et al.* (US 6,620,198).

On page 13 of the Office Action, the examiner rejects the claims 175-180 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315) in view of Burstein *et al.* (US 6,620,198), as applied to claim 170 above, and further in view of Mckellop *et al.* (WO 99/52474).

On page 14 of the Office Action, the examiner rejects the claim 186 under 35 U.S.C. 103(a) allegedly as being unpatentable over Lidgren *et al.* (US 6,448,315), in view of Burstein *et al.* (US 6,620,198), as applied to claim 182 above, in further view of Saum *et al.* (US 2002/0107300).

Applicants respectfully disagree with the examiner and submit that the cited references do not teach or suggest all claim limitations of the independent claims and refer to the MPEP that:

> "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).
>
> *See*, MPEP § 2143.03 at 2100-142 (Rev. 6, September 2007).

> Not only must all of the elements recited in the claim be present, the elements must be "arranged or combined in the same way" as recited in the claim in order for anticipation to be found. *Net MoneyIN Inc. v. VeriSign Inc.,* 545 F.3d 1359, 1369-71, 88 USPQ2d 1751, 1758-59 (Fed. Cir. 2008).

Applicants point out, as admitted by the examiner on page 3 of the Office Action, the instant application and Lidgren *et al.* do not do the claimed steps in order, accordingly a *prima facie* case of obviousness is not established.

However, in order to assist the examiner in distinguishing the claimed invention from the cited references applicants submit the following clarifications that the claimed inventions are not obvious in view of Lidgren *et al.* (US 6,448,315), and further in view of Burstein *et al.* (US 6,620,198), and/or Mckellop *et al.* (WO 99/52474), and/or Muratoglu *et al.* (US 2003/0149125), and/or Saum *et al.* (US 2002/0107300).

Lidgren's process is different:

Lidgren requires doping of vitamin E in presence of supercritical CO_2 (see col. 3, lines 43-62, for example). However, instant claims do not recite doping in a supercritical fluid or CO_2.

Lidgren does not teach annealing of mechanically deformed cross-linked polymeric blend or warm irradiation to prevent oxidation.

In addition, Lidgren does not teach the use of consolidated forms of polymeric blend nor does it teach about the effects of irradiation on consolidated forms with vitamin E.

On page 16 of the Office Action, in response to the arguments, the examiner asserted that:

> "While Lidgren *et al.* (US '315) employs a supercritical CO2 diffusion doping process, the instant claims fail to exclude such a process, therefore any process can be employed which introduces the additive into the polymeric material."

Applicants disagree with the examiner and point out that the instant independent claims recite polymeric blends and do not involve doping of powder in supercritical fluid

conditions, as stated by the examiner. Dependent claims 138-139 recite doping of polymeric blends (blended with antioxidants *per se*). Whereas, the examiner is referring to Lidgren's mixing of UHMWPE powder as the doping step which requires a solvent comprising CO_2 under supercritical conditions (see Lidgren Col. 4, lines 45-50, for example, also referred by the examiner). In contrast, instant claim step of mixing or blending, as the case may be, the polymeric material with one or more additives is a step for preparing the polymeric blend, and not a doping process. That is, a "blending" process is not the same as a "doping" process, which are clearly defined in the specification (see pages 57-60). Accordingly, Lidgren's doping process is different and the instant claims do not recite doping a powder in a supercritical fluid or CO_2.

Saum teaches away:

Saum actually discourages one from using antioxidants or additive generally. Applicants refer the examiner to Saum's disclosure that states: "The UHMWPE preform material does not contain stabilizers, antioxidants, or other chemical additives which may have potential adverse effects in medical applications." (see page 2, at [0012]). Thus, Saum teaches away from using additives generally. *See In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994) (stating, "[a] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant"). Therefore, by reading Saum, one skilled in the art would not consider use of an additive. Thus, there is no motivation to combine Saum in order to rectify the deficiencies of Lidgren.

Regarding a radiation process, Saum teaches low dose radiation for sterilization and not for cross-linking. Saum states: "By separating the irradiation cross-linking step from the sterilization step, the current invention allows one to use lower levels of irradiation for cross-linking than would be effective for sterilization of UHMWPE." (see page 1, at [0008]).

The examiner admits that Saum does not teach the irradiation step after the heating/pressurization process, that is, Saum also does not teach the claimed process

steps in the same order of instant claims, for example, claim 155. Thus, a combination with Lidgren would not make the claimed invention obvious.

McKellop is not a relevant art:

Applicants submit that Mckellop disclosure is not relevant to the claimed invention. McKellop's process involves blending with peroxide, which does not make oxidation-resistant polyethylene. Peroxide is a chemical cross-linking agent not an antioxidant. In contrast, additives such as antioxidants used in the claimed invention are not cross-linking agents. In this context, applicants herewith provide a copy of the inventor Dr. Orhun Muratoglu's earlier research publication showing the effect of peroxide on UHMWPE (see Muratoglu *et al.* 1997, Abstract, page 49, 23 Annual Meeting of the Society for Biomaterials, April 30 to May 4, 1997). The research publication concludes that "[t]he unassociated peroxides left in peroxide cross-linked UHMWPE may result in long-term oxidation of the cross-linked polymer. On the other hand, the irradiation of UHMWPE with melting either during or subsequent to cross-linking (MIR) and CISM) will lead to no long-lived free radicals which are the known cause of long-term degradation." (see Muratoglu *et al.* 1997, page 49, right column last paragraph of the article and Figures 1 and 2, for example). Thus, publication clearly demonstrates that peroxide is a cross-linking agent, which also makes the polymeric material prone to oxidation. Accordingly, McKellop's blending with peroxide does not provide a method of making oxidation-resistant polymeric material.

Applicants also point out, unlike the claimed process, McKellop utilizes the peroxide as a free radical generating chemical (see page 4, lines 2-8, for example), a chemical cross-linker (see page 24, line 5 to page 25 line 10, for example), which is removed after the cross-linking step (see page 23, lines 30-32, for example). In the instant claimed methods, the additives are blended to make the polymeric material oxidation-resistant, are not used for chemical cross-linking, and are not used as a free radical generating chemical. In view of the above, applicants submit that the McKellop disclosure is not relevant to the claimed invention and a combination with any other cited references is improper.

McKellop, Burstein and Muratoglu:

McKellop does not rectify the deficiencies of Lidgren.

McKellop's process involves blending with peroxide, which does not make oxidation-resistant polyethylene, as clarified above. Therefore, a combination of McKellop with Burstein and/or Lidgren would not make the claimed invention obvious.

As explained above, Burstein and/or Muratoglu (US 2003/0149125) do not rectify the deficiencies Lidgren. Therefore, a combination of Burstein or Muratoglu with Lidgren does not make the claimed invention obvious.

Accordingly, a combination of Lidgren with Burstein and Saum or McKellop would not make the claimed invention obvious.

Applicants have explained above, even if the cited references were combined, would not yield the claimed method nor the claimed medical implant. Besides, as clarified above, Saum teaches away from using a key ingredient, additive (antioxidant), and thus actually discredits Lidgren. McKellop, Burstein, Saum or Muratoglu does not rectify the deficiencies of Lidgren, as discussed above. Therefore, any combination of the cited references would not yield the claimed process.

In view of the above, applicants submit that a *prima facie* case of obviousness has not been established. Accordingly, withdrawal of the obviousness rejection is earnestly requested.

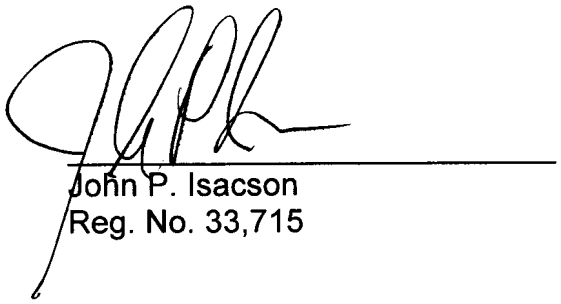
Double Patenting Rejection:

On pages 14-15 of the Office Action, the examiner provisionally rejects claims 125-127, 132-133 on the ground of non-statutory obviousness-type double patenting allegedly as being unpatentable over claims 72, 74, 63, 80-81, 86 of co-pending application No. 11/465,509. Applicants submit that since a notice of allowability has not been issued for the co-pending application, the merits of this provisional rejection need not be discussed with the examiner at this time. *See* MPEP § 822.01.

REQUEST

Applicants submit that claims 125-186 are in condition for allowance and request consideration to that effect. The examiner is invited to contact the undersigned at 202-628-6600 should there be any questions.

Respectfully submitted,



May 24, 2010
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LONG TERM STABILITY OF RADIATION AND PEROXIDE CROSS-LINKED UHMWPE

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Introduction: The wear of ultra-high molecular weight polyethylene (UHMWPE) components used in total joint arthroplasty remains one of the major causes of osteolysis related loosening and failure. One method of improving the wear resistance of polyethylenes is cross-linking through peroxide [1], silane [2], or radiation chemistry [3,4]. These methods could, however, jeopardize the long-term oxidative stability of the material. Both the peroxide and silane methods result in residual un-dissociated peroxides that could dissociate in the long-term and lead to the embrittlement of the polymer. Similarly, the radiation techniques result in trapped free radicals that would eventually take part in the long-term oxidation reactions. The radiation cross-linked polymers could be mobilized, e.g. by heating above the melting temperature, to eliminate the persisting free radicals through recombination processes [5]. In this study we evaluated the long term stability of radiation and peroxide cross-linked UHMWPE by electron spin resonance and thermo-oxidative aging techniques.

Materials and Methods: The cross-linked UHMWPEs used in this study were as follows: (i) peroxide cross-linked Himont 1900 resin provided by Poly Hi-Solidur (PXL), (ii) GUR 4150 bar stock irradiated in the molten state to 200kGy with a 3MeV Van de Graaf electron beam generator (IMS), (iii) GUR 4150 bar stock irradiated to 25, 40, 50, 100, and 200kGy (e-beam) at a dose rate of 3kGy/min in air, followed by heating to 150°C for 2 hours under vacuum and cool down to room temperature at a rate of -10°C/min (CISM). The irradiation of CISM was carried out with a 10 MeV electron beam (AECL, Pinawa, Canada) operated at 1kW. The radiation treated specimens (IMS and CISM) along with a control specimen (GUR 4150 irradiated to 25kGy in air) were analyzed using electron spin resonance to qualitatively determine the final free radical concentrations. The long-term stability of the PXL and CISM materials was evaluated by thermooxidative aging at 75°C under 1500 psi of O_2 pressure in a bomb reactor. The PXL and CISM specimens were microtomed into thin (50μm) sections which were aged in the bomb reactor. The specimens were removed from the aging reactor at 3 day intervals. The oxidation levels were determined using a BioRad infra-red spectrometer.

Results and Discussion: The UHMWPE irradiated to 25kGy in air showed peroxy free radicals as measured by EPR (24 days after irradiation). The EPR experiments on radiation treated UHMWPE using the MIR and CISM methods showed no detectable free radicals. The thermooxidative aging behavior of the PXL and the CISM materials are shown in Figures 1 and 2 as a function of aging time. The early onset of oxidation in peroxide cross-linked polymer shows that peroxide cross-linking may in the long-term result in oxidative instability of the polymer.

As expected irradiation of UHMWPE at room temperature (in air) to 25kGy led to the formation of trapped free radicals. Upon melting (CISM), independent of the total absorbed radiation dose, the concentration of trapped free radicals decayed to undetectable levels (by EPR). Similarly, the MIR method resulted in no detectable free radicals. Figure 2 shows the thermooxidative aging of CISM of various absorbed dose levels along with an unirradiated control and a cold irradiated (25kGy) UHMWPE control. This figure indicates that the melting of an irradiated UHMWPE improves its thermooxidative stability

Cross-linking by various methods is known to improve the wear resistance of UHMWPE. However, special care must be taken in evaluating the long-term stability of the cross-linked polymer. The undissociated peroxides left in peroxide cross-linked UHMWPE may result in long-term oxidation of the cross-linked polymer. On the other hand, the irradiation of UHMWPE with melting either during or subsequent to cross-linking (MIR and CISM) will lead to no long-lived free radicals which are the known cause of long-term degradation.

References: 1. Himont Tech. Info. Bull. HPE-116 (1987). 2. Wroblewski et al. JBJS 78-B(2):280-285 3. McKellop, H., Harv. Med. Schl. Hip Cse. (1996). 4. Jasty, M. et al., Harv. Med. Schl. Hip Cse. (1996). 5. Dickson, L. W., AECL Info. Bull AECL-9556 (1988).

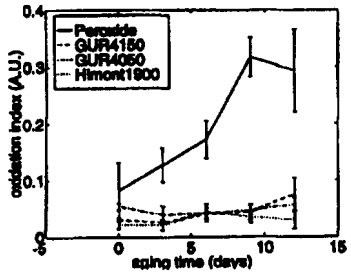

Figure 1.

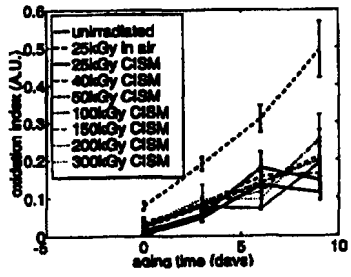

Figure 2.

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